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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/887,496	BANERJEE ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-21,23-38,40-64,69-74,78-83,87-89 and 99-146* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1,3-21,23-38,40-64,69-74, 78-83, 87-89, 93, 99-146* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/04/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/04/2008 has been entered.

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93 and 99-146 are pending, and examined herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 99-112, 117-119, and 122-128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hochrainner et al. (US 6,150,418, PTO-892 of record) in view of Carling et al. (US 5,674,860, PTO-892 of record), and PDR.

Hochrainner et al. discloses propellant-free pharmaceutical composition comprising formoterol or its salt, or addition products (preferably, formeterol fumarate as salt, hydrate as addition product), a known bronchodilator, particularly stable on storage with concentration 10 –500 mg/ml (see col.1, lines 37-46, lines 65-67; col.2 lines 6-11), in aqueous ethanol, and ethanol mixture (water and ethanol are well known polar and protic solvents, see col.2 lines 24-34), in the form of a solution or suspension for use in inhalers for nasal therapy, see abstract and claims 1-4, 8 in particular. Hochrainer et al. further teaches that the pharmaceutical composition is such that it can be administered by inhalation using a suitable nebuliser, see col.4, lines 19-20 and col. 5, lines 33-41. Hochrainer et al. teaches that the pH range is preferably between 2.0-7.0 and most preferably between 4.5-5.5. The employment of inorganic acids, and organic acids such as phosphoric acids, citric acid, tartaric acid, fumaric acid etc. and the employment of buffers in its composition are also taught, see in particular col.3, lines 35-40 and col.4 line 55 to col. 5, line 7; and inorganic salts, sodium chloride, and organic salts such as for example, sodium, potassium or ammonium salts of citric acid, Na-EDTA (see col.2 lines 56-64, col. 4, lines 55-57) in the composition is also taught. Hochrainer et al. teaches the concentration of formoterol to be between about 75 mg/ml and about 500 mg/ml, which may be used with diluent, and other ingredients for the preparation of therapeutical composition. See in particular claims 1-4. Hochrainer et al. also teaches that additional active ingredients such as steroids, antichlolinergics could be incorporated in its composition, see claim 19. It is taught that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance

concentrate with a pharmacologically suitable solvent. See column 4, lines 21-25. It is taught that the formulation for administration is obtained by diluting to 0.9 mg/ml of formoterol with the diluents such as water, aqueous saline and the PH is adjusted for stable storage. See column 4, lines 26-29; column 5, lines 1-6. A formulation containing a solvent mixture of ethanol/water, formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5 is also disclosed. See column 8, claim 22. The pharmaceutical compositions therein can contain surfactants for stabilizing suspensions or other stabilizers which include sorbitan esters which reads on instant Polysorbate 80. See column 3, lines 10-27.

Hochrainer et al. also discloses a kit or an article of manufacture comprising the same combination and packaging material include containers, nebulizers. Preferred nebulizers include inhalers. See column 5, lines 33-47. The compositions therein are employed in the methods of treating obstructive respiratory diseases and asthma, see col. 1, lines 1- 37.

Hochrainer et al. does not teach particularly the employment of a steroidal anti-inflammatory agent, fluticasone propionate, and its concentration.

Hochrainer et al. does not explicitly teach the concentration of formoterol such as 5 μg/ml to about 200 μg/ml, 50 μg/ml to about 200 μg/ml, 59 μg/ml, 118 μg/ml in its pharmaceutical composition, and does not expressly teach the concentration of buffer providing particular PH value, and the ionic strength of the composition.

Carling et al. discloses a pharmaceutical composition comprising formoterol (free base) or formoterol fumarate salt in combination with corticosteroid anti-inflammatory

agent, budesonide, in a pharmaceutically acceptable fluid such as a liquid (see col.4 line 2), by inhalation from a nebulizer (see col.3 line 51) for the treatment of respiratory disorders such as asthma (see title and abstract, col.1 lines 10-15, 46-67). Carling et al. also discloses the effective amount of formoterol, 6-100 μg, preferred 6-48 μg (the instant claimed amount within the range of Carling et al.), in a pharmaceutical composition therein (see col.3 lines 44-45). Carling et al. also discloses that a pharmaceutical composition of the combination therein is formulated into a single dosage administration (see Example 1-3 at col.4). Carling et al. also discloses a kit or an article of manufacture comprising the same combination and a nebulizer (see col.3 line 8-10 and 50-52, claims 1-36). Carling et al. also discloses the employment of a tonicity adjusting agent herein such as salts of inorganic or organic salts, e.g., succinate, lactate (see col.3 lines 30-38) and adding oleic acid may improve the physical stability (see col.4 line 12-14).

PDR teaches fluticasone propionate as a known corticosteroid readily employed in the method of treating asthma.

From the teaching of PDR, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ fluticasone propionate in the composition of Hochrainer et al. It is prima facie obvious to combine two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. The optimization of a result effective parameter, e.g., the effective amounts of active ingredients and excipients in a therapeutical dosage form, is considered within the skill

of the artisan. See, In re Boesch and Slanev (CCPA) 204 USPQ 215. The skilled artisan would see a container as a vial useful for multiple uses, absent information the contrary.

It would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as the concentration of formoterol in its pharmaceutical composition, and the concentration of buffer providing particular PH value, and the ionic strength of the composition. The optimization of a result effective parameter, e.g., the effective amounts of active ingredients and excipients in a therapeutical dosage form, is considered within the skill of the artisan. See, In re Boesch and Slanev (CCPA) 204 USPQ 215.

With regard to the limitations "whereby the composition has an estimated shelf-life of greater than 1 month usage time at 25 °C and greater than or equal to 1 year storage time at 5 °C, "whereby greater than 90 % of the initial amount of formoterol in the composition remains at such time", and "the composition is formulated for direct administration", Hochrainer et al. disclose a formulation containing a solvent mixture of ethanol/water, formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5, and further teaches that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance concentrate with with polar solvents such as water, aqueous saline and adjusting the PH to obtain a stable formulation. See column 8, claim 22. The compositions therein can contain steroids. Thus, absent showing unexpected, and significant benefit residing in the particular limitations herein, the claimed invention would have been obvious to one of skill in the art. Hochrainer et al. particularly teach that the concentrated solution may be

used for making pharmaceutical composition which is such that it can be administered by inhalation using a suitable nebuliser, see col. 4, lines 19-20 and col. 5, lines 33-41. Therefore, it would have been obvious to make a diluted formoterol solution suitable for direct administration. It is noted that fluticasone is not water soluble, therefore, a suspension of fluticasone would have been obvious to one of ordinary skill in the art.

Claim 93 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hochrainner et al. (US 6150418, PTO-892 of record) in view of Carling et al. (US 5674860, PTO-892 of record), and PDR, and further in view of PDR at pages 482, 535, 537, 2828 (of record).

The same disclosures of Hochrainner et al. in view Carling et al. (US 5674860), and PDR have been discussed in the 103(a) rejection set forth above.

Hochrainner et al., Carling et al. do not expressly disclose further adding one or more agent recited in claim 93 herein to the composition.

PDR teaches that albuterol (beta2-adrenoreceptor agonist), accolate (leukotriene receptor antagonist) and Zyflo (5-lipoxygenase inhibitor) are all known to be effective in treating asthma.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a third active such as those enumerated immediately above in a combination composition along with formoterol and fluticasone.

One of ordinary skill in the art would have been motivated to employ a third active such as those enumerated immediately above in a combination composition

along with formoterol and fluticasone because all three actives are known to be useful in treating asthma. Combining two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Claims 113-116 and 120-121 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hochrainner et al. (US 6150418, PTO-892 of record) in view of Carling et al. (US 5674860, PTO-892 of record), and PDR, and further in view of Hardman et al. (Goodman Gilman 's *The Pharmacological Basis of Therapeutics*,1996, page 665, of record) or Leckie et al (*Novel Therapy* Of COPD, abstract, Jan 2000, of record).

The same disclosures of Hochrainner et al. in view Carling et al. (US 5674860, and PDR have been discussed in the 103(a) rejection set forth above.

Hochrainner et al., Carling et al. and PDR do not expressly disclose further adding an anticholinergic agent such as ipratropium bromide or tiotropium bromide to the composition therein.

Hardman et al. teaches that ipratropium bromide is an anticholinergic agent useful in treating asthma.

Leckie et al teaches that tiotropium is a known bronchodilator employed in treatment of asthma.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a third active such as ipratropium bromide or tiotropium bromide in a combination composition along with formoterol and fluticasone.

One of ordinary skill in the art would have been motivated to employ a third active such as ipratropium bromide or tiotropium bromide in a combination composition along with formoterol and fluticasone because all three actives are known to be useful in treating asthma. Combining two agents which are known to be useful to treat asthma individually into a single composition useful for the very snme purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Claims 129-146 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hochrainner et al. (US 6,150,418, PTO-892 of record), in view of Remington's Pharmaceutical Sciences, Seventeenth Edition, 1985, pages 1443, 1451.

Hochrainner et al. discloses propellant-free pharmaceutical composition comprising formoterol or its salt (preferably, formeterol fumarate), a known bronchodilator, particularly stable on storage with concentration 10 –500 mg/ml (see col.1 line 65-67; col.2 line 6-11), in aqueous ethanol (water and ethanol are well known polar and protic solvents, see col.2 lines 24-34), in the form of a solution or suspension for use in inhalers for nasal therapy, see abstract and claims 1-4, 8 in particular. Hochrainer et al. further teaches that the pharmaceutical composition is such that it can be administered by inhalation using a suitable nebuliser, see col.4, lines 19-20 and col. 5, lines 33-41. Hochrainer et al. teaches that the pH range is preferably between 2.0-7.0 and most preferably between 4.5-5.5. The employment of inorganic acids, and organic acids such as phosphoric acids, citric acid, tartaric acid (i.e addition of tartaric acid to formoterol, results in instant formoterol tartrate), fumaric acid etc and the employment of

buffers, e.g. phosphate buffers, in its composition are also taught, see in particular col.3, lines 35-40 and col.4 line 55 to col. 5, line 7; and inorganic salts, sodium chloride, and organic salts such as for example, sodium, potassium or ammonium salts of citric acid (see col.2 lines 56-64) in the composition is also taught. Hochrainer et al. teaches the concentration of formoterol to be between about 75 mg/ml and about 500 mg/ml, which may be used with diluent, and other ingredients for the preparation of therapeutical composition. See in particular claims 1-4. Hochrainer et al. also teaches that additional active ingredients such as steroids, antichlolinergics could be incorporated in its composition, see claim 19. It is taught that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance concentrate with a pharmacologically suitable solvent. See column 4, lines 21-25. It is taught that the formulation for administration is obtained by diluting to 0.9 mg/ml of formoterol with the diluents such as water, aqueous saline and the PH is adjusted for stable storage. See column 4, lines 26-29; column 5, lines 1-6. A formulation containing a solvent mixture of ethanol/water, formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5 is also disclosed. See column 8, claim 22.

Hochrainer et al. also discloses a kit or an article of manufacture comprising the same combination and packaging material which include containers, nebulizers. Preferred nebulizers include inhalers. See column 5, lines 33-50. The compositions therein are employed in the methods of treating obstructive respiratory diseases and asthma, see col. 1, lines 1- 37.

Hochrainer et al. does not explicitly teach the concentration of formoterol such as 5 μg/ml to about 200 μg/ml, in its pharmaceutical composition, and does not expressly teach the concentration of buffer providing particular PH value.

It would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as the concentration of formoterol in its pharmaceutical composition, and the concentration of buffer providing particular PH value. The optimization of a result effective parameter, e.g., the effective amounts of active ingredients and excipients in a therapeutical dosage form, is considered within the skill of the artisan. See, In re Boesch and Slanev (CCPA) 204 USPQ 215. Note, sterility of a pharmaceutical composition is an essential element in the practice of pharmacy, and thus is deemed to be obvious. See Remington's Pharmaceutical Science, pages 1443, 1451 attached herein. Also, note that the skilled artisan would see a container as a vial useful for multiple uses, absent information to the contrary.

With regard to the limitations "whereby the composition has an estimated shelf-life of greater than 1 month usage time at 25 °C and greater than or equal to 1 year storage time at 5 °C, "whereby greater than 90 % of the initial amount of formoterol in the composition remains at such time", and "the composition is formulated for direct administration", Hochrainer et al. disclose a formulation containing a solvent mixture of ethanol/water, formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5, and further teaches that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance concentrate with with polar solvents such as water, aqueous saline and adjusting the PH to obtain a

stable formulation. See column 8, claim 22. The compositions therein can contain steroids. Thus, absent showing unexpected, and significant benefit residing in the particular limitation herein, the claimed invention would have been obvious to one of skill in the art. Hochrainer et al. particularly teach that the concentrated solution may be used for making pharmaceutical composition which is such that it can be administered by inhalation using a suitable nebuliser, see col. 4, lines 19-20 and col. 5, lines 33-41. Therefore, it would have been obvious to make a diluted formoterol solution suitable for direct administration. It is noted that fluticasone is not water soluble, therefore, a suspension of fluticasone would have been obvious to one of ordinary skill in the art.

Response to Arguments

Applicant's amendments and remarks have been fully considered, but are not found persuasive.

Applicant's remarks on issued patents have been considered. The examiner maintains that issued U.S. Patent is a property, not a precedent. It is pointed out that the examiner will not make any comment on issued US patent.

Applicant argues that "Applicants note-that the compositions containing formoterol in solution and steroidal anti-inflammatory in suspension as recited in claim I are surprisingly and unexpectedly stable. Typically, formulations having one drug in solution and one drug in suspension are not stable. Thus, in order to obtain a stable formulation, usually both drugs are provided either in suspension or in solution. Even Hochrainer teaches that the formoterol can be in solution or suspension, but does not

disclose formulations having one drug in solution and another in suspension. In contrast, the present application provides that the formoterol is in solution and the steroidal anti-inflammatory is in suspension." These arguments have been considered, but not found persuasive. Hochrainner et al. discloses propellant-free aqueous pharmaceutical composition comprising formoterol or its salt (preferably, formeterol fumarate), a known bronchodilator, in the form of a solution or suspension for use in inhalers for nasal therapy. PDR teaches fluticasone propionate as a known corticosteroid readily employed in the method of treating asthma. From the teaching of PDR, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ fluticasone propionate in the composition of Hochrainer et al. It is prima facie obvious to combine two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. As the combined teachings of the prior art renders the claimed composition obvious, the property of such a claimed composition will also be rendered obvious by the prior art teachings, since the properties, namely the formoterol in solution and steroid in suspension in propellant-free water, are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See MPEP 2112.01. It is noted that fluticasone is not water soluble, therefore, a suspension of fluticasone would have been obvious to one of ordinary skill

in the art. Further, note that the instant claims 129-146 do not contain a steroidal anti-inflammatory agent.

Applicant argues that "Hoehrainer teaches that compositions containing 900 μ g/mL would not be stable for long term storage." These arguments are not persuasive. It is pointed out that Hoehrainer does not teach that compositions containing 900 μ g/mL would not be stable for long term storage.

Hoehrainer teaches formulation containing a solvent mixture of ethanol/water, and formoterol in a concentration of about 0.9 to about 1.5 mg/ml. Carling et al. also discloses the effective amount of formoterol, 6-100 μg, preferred 6-48 μg (the instant claimed amount within the range of Carling et al.), in a pharmaceutical composition. Accordingly, it would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as the concentration of formoterol in its pharmaceutical composition. The optimization of a result effective parameter, e.g., the effective amounts of active ingredients in a therapeutical dosage form, is considered within the skill of the artisan. See, *In re Boesch*.

Further, it is noted the particular concentration recited in Hochrainer is merely "for example", and is not a requirement. It is well-settled that disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Further, Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions

of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955).

As to the asserted superiority of the claimed invention, i.e., a long stable composition, applicants appear to argue an unexpected benefit residing in claimed invention. Regarding the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be unexpected and significant. See MPEP 716.02 (b). The claims must be commensurate in the scope with any evidence of unexpected results. See MPEP 716.02 (d). Further, A DECLARATION UNDER 37 CFR 1.132 must compare the claimed subject matter with the closest prior art in order to be effective to rebut a prima facie case if obviousness. See, MPEP 716.02 (e).

Applicant argues that “The Examiner recognized that Hochrainer does not teach compositions with steroid in suspension in propellant-free water, and cited Carling, PDR, Hardman, Leckie and Remington's Pharmaceutical Services to teach those elements. Applicants respectfully submit that these secondary references do not cure the deficiencies of Hochrainer, and thus, would not lead one of skill in the art to the present invention.” These arguments have been considered, but not found persuasive. It is pointed out that Carling, PDR, Hardman, Leckie are employed for their teachings that fluticasone propionate, albuterol, ipratropium bromide or tiotropium bromide etc. are well known to be used for treating asthma. Accordingly, it would have been obvious to a person of ordinary skill in the art at the time of invention to employ a steroidal anti-

inflammatory agent, fluticasone propionate, albuterol, ipratropium bromide or tiotropium bromide in the composition taught by Hochrainer et al. It is prima facie obvious to combine two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93, 99-146 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of US Application No. 11/688436 in view of Carling et al., PDR, and further in view of Remington.

US Application No. 11/688436 claims a pharmaceutical composition comprising (R) formoterol or a salt thereof at a concentration of from about 0.08 µg/mL to about 43 µg/mL based on formoterol free base, in a pharmacologically suitable solution, wherein the composition further comprises water and a buffer. '436 does not expressly claim the employment of steroidal anti-inflammatory agent. However, the employment of such

agent would have been obvious in view of the secondary references for reasons as discussed in the obvious rejection above. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ fluticasone propionate in the instant pharmaceutical composition. It is prima facie obvious to combine two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. Note, sterility of a pharmaceutical composition is an essential element in the practice of pharmacy, and thus is deemed to be obvious. See Remington's Pharmaceutical Science.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93, 99-128, 129-146 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 7,348,362 in view of Carling et al., PDR. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to substantially overlapping pharmaceutical compositions.

U.S. Patent No. 7,348,362 claims a pharmaceutical composition comprising formoterol or a salt thereof at a concentration of from about 0.08 µg/mL to about 34 µg/mL based on formoterol free base, in a pharmacologically suitable solution, wherein the composition further comprises water and a buffer. '362 does not expressly claim the

employment of steroidal anti-inflammatory agent. However, the employment of such agent would have been obvious in view of the secondary references for reasons as discussed in the obvious rejection above. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ fluticasone propionate in the instant pharmaceutical composition. It is prima facie obvious to combine two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93, 99-146 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-88 of U.S. Patent No. 6,667,344 in view of Carling et al., PDR. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to substantially overlapping pharmaceutical compositions.

US Patent 6,667,344 claims a pharmaceutical composition comprising formoterol or a derivative thereof formulated at a concentration suitable for direct administration to a subject in need thereof, in a pharmacologically suitable fluid, wherein the composition is stable during long term storage and the fluid comprises water, wherein the composition may further comprising other active ingredient(s). '344 does not expressly claim the employment of steroidal anti-inflammatory agent. However, the employment of such agent would have been obvious in view of the secondary references for reasons as discussed in the obvious rejection above. It would have been obvious to one of

ordinary skill in the art at the time the invention was made to employ fluticasone propionate in the instant pharmaceutical composition. It is prima facie obvious to combine two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93, 99-146 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-73 of U.S. Patent No. 6,814,953 in view of Carling et al., PDR. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to substantially overlapping pharmaceutical compositions.

US Patent 6,814,953 claims a kit comprising formoterol or a derivative thereof formulated at a concentration suitable for direct administration to a subject in need thereof, in a pharmacologically suitable fluid, wherein the composition is stable during long term storage and the fluid comprises water, wherein the composition may further comprising other active ingredient(s). '953 does not expressly claim the employment of steroidal anti-inflammatory agent. However, the employment of such agent would have been obvious in view of the secondary references for reasons as discussed in the obvious rejection above. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ fluticasone propionate in the instant pharmaceutical composition. It is prima facie obvious to combine two agents which are

known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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